Rec'd PCT/PTO 25 APR 2005
PCT/GB 2003 / 0 0 4 7 0 6

10/532521

The Patent Office

INVESTOR IN PEOPLE

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN COMPLIANCE WITH RULE 17.1(a) OR (b)

REC'D 02 MAR 2004
WIPO PCT

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed [signature]

Dated 23 February 2004

Patents Form 1/77

Patents Act 1977
(Rule 16)

The Patent Office

01NOV02 E760438-1 C91014
P01/7700 0.00-0225498.5

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

THE PATENT OFFICE
A
- 1 NOV 2002
RECEIVED BY FAX

The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference — FINAL JET

2. Patent application number *(The Patent Office will fill in this part)* — 0225498.5 — 01 NOV 2002

3. Full name, address and postcode of the or of each applicant *(underline all surnames)* — WILLIAM ANTHONY DENNE, THE LANE HOUSE, 10B CHURCH STREET, GREAT SHELFORD, CAMBRIDGE CB2 5EL UK.

   Patents ADP number *(if you know it)* — 3284502001

   If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention — IMPROVED JET INJECTOR

5. Name of your agent *(if you have one)* — AS IN 3 ABOVE

   "Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

   Patents ADP number *(if you know it)*

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*
PCT	/GB02/02633	19 JUN 02

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*
N/A	

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*
   a) any applicant named in part 3 is not an inventor, or
   b) there is an inventor who is not named as an applicant, or
   c) any named applicant is a corporate body.
   See note (d)) — NO

0051626 01-Nov-02 06:38

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	0
Description	5
Claim(s)	0
Abstract	1
Drawing(s)	5

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*

Request for preliminary examination and search *(Patents Form 9/77)*

Request for substantive examination *(Patents Form 10/77)*

Any other documents *(please specify)*

N/A

11. I/We request the grant of a patent on the basis of this application.

Signature W. A Denne Date 1 NOV 02

12. Name and daytime telephone number of person to contact in the United Kingdom 01223 846191

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) *If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.*

b) *Write your answers in capital letters using black ink or you may type them.*

c) *If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.*

d) *If you have answered 'Yes' Patents Form 7/77 will need to be filed.*

e) *Once you have filled in the form you must remember to sign and date it.*

f) *For details of the fee and ways to pay please contact the Patent Office.*

0051626 01-Nov-02 06:38

IMPROVED JET INJECTOR

PCT / GB 02 / 02633 describes a jet injector in which there is a rigid tube terminating at one end in a nozzle and at the other in a constriction which leads to the main drug supply. A portion of the rigid tube is formed as a flexible window. There is an over centre spring which may deliver a hammer blow to the window to cause a high speed flow through the nozzle and a more gradual acceleration of drug through the constriction. The jet pierces the skin of the patient to cut a track and the main dose may be delivered manually down this track. The present specification details a number of improvements in the design of this device

According to the present invention, there are a number of improvements to the jet injector specified in PCT / GB 02 / 02633 which are as follows. Rather than energising the spring by pressing against the skin of the patient, the profile of load with displacement may be made asymmetric so that the spring is energised manually and triggered by pressure on the skin of the patient. The spring may be in the form of one of more C springs deforming by bending in the plane of the axis of the injector. The C profile may be modified toward an L or J shape if required. The C spring may be retained by a cross member that seats in a transverse channel at the base of a retaining wall. The cross member may engage with the flexible portion of the rigid tube via a small cross section piston. The flexible portion of the rigid wall may be formed as a rubber liner within the rigid tube that is accessed via an open window within the rigid tube wall. The rubber liner may incorporate a non-return valve that is normally closed or is biassed in the closed position. The rubber liner may be free or bonded to the constriction for ease of assembly. The outer surface of the nozzle may be such that it induces a saddle shape in the skin it impresses in order to maintain the entrance to the track through the skin in the open position.

In the original specification, it was stipulated that the device was energised by pressure against the skin of the patient. The spring reached the unstable maximum strain configuration then spontaneously accelerated to impact. There was facility within the design to constrain the load-displacement profile of the spring between the limits of travel. If these limits are set extremely asymmetrically, the spring is effectively energised by manually cocking the device and then triggered by pressure against the skin of the patient. As human fingers have evolved to comfortably exert much larger forces that most of the skin, this arrangement permits a much larger spring energy and reduced loading on the skin of the patient. This arrangement also provides greater design flexibility within the limited space available.

The spring outlined in PCT / GB 02 / 02633 deformed by shear and stretching. Such an arrangement on a small scale leads to a rigid spring design of limited deflection and limited energy. The limited deflection leads to difficult fabrication tolerances. Bending strain offers greater deflection and the potential for greater energy storage. In the cited priority documents, circular springs are described which bend about two axes simultaneously. While such devices provide greater flexibility, the biaxial bend constraint substantially reduces the energy that may be stored within the material strain limits. A C spring provides bending strain but in one plane only. Figure 1a shows such a spring, 106, in side view and in end elevation in figure 1b. There are two C shaped elements, which are disposed symmetrically about the injector body, and are bonded rigidly by cross beams,104 and 110, at their ends. One cross beam, 110, pivots freely while the other is attached rigidly a triangular cross member, 105, which may pivot in a transverse channel, 107, to extend the spring. Figure 1c shows

the C spring in the extended mode. The restraining wall, 108, prevents further rotation and the rear wall of the pivot channel, 107, provides a reaction, so that the spring assembly is securely retained.

The configuration of figure 1c is clearly at maximum spring strain. By placing the lower pivot point, 121, slightly forward of the pivot channel, 107, a forward rotation moment is generated which latches the spring against the restraining wall, 108. It is important there is no bending moment between the spring, 106, and the cross member, 105, that upsets this latching. During the stretching of the C spring, there is rotation of the cross member, bodily rotation of the spring and splaying of the spring. In figures 1d and 1e, the initial and final spring curvatures are shown schematically as curves 102 and 103 respectively. Figure 1d shows the bodily rotation angle, 101. Figure 1e shows the splay angle, 100, on extension of the spring. It may be shown that the angle between the cross member and spring first decreases then increases with extension of the spring. There is always a configuration at full extension where there is no change in this angle and therefore no additional bending moment due a distortion of the angle between cross member and spring.

While C springs have been considered so far, the profile of the spring may be redesigned as closer to an L or J configuration, without changing the essential mechanics. This may permit a larger spring in a confined design space.

In PCT/GB02/02633 a double sided system is presented. A single sided system offers more design flexibility and eliminates timing problems on impact.

The end thrust member, 105, may have a peg, 109,, of small smaller cross section that may act as a piston driving the flexible window, 111, in a hole of similar size. In this fashion a given impact force may produce a much higher impact pressure within the rigid tube.

To form a flexible window, 111, within the wall of a rigid tube, 120, requires a delicate priming and moulding operation with the risk of flash, 130, within the channel. The flash may break away to block the nozzle, 131. A simpler arrangement is shown in section in figure 2. There is an open window, 20, in the rigid wall, 9, and a rubber liner, 21, within the rigid tube. When the piston impacts on the liner, the pressure within the tube increases, reinforcing the seal of the liner against the inner surface of the rigid tube wall. The forces on the liner are essentially isotropic, so despite the extremely high hydraulic pressure transient, there will be no damage to the rubber. The liner may also incorporate a slit non-return valve, 22. This may be closed in the quiescent state or even biassed in the closed position by the seating pressure of the rubber liner. With such a valve, there can be no reverse flow down the constriction, 23, so the transient pressure will be higher and the volume pumped through the nozzle will be greater. Further, thermal contraction of fluid in the attached drug ampoule cannot withdraw fluid from the pump chamber so ambient thermal cycling will not interfere with priming of the pump. The liner cum non-return valve may be free standing but is preferably bonded to the inner face of the constriction, 23. The constriction is still required to given support to the non return valve and ensure a small dead volume on the pump stroke. However, the length may be attenuated as there is no longer the need to have a large column of fluid to impede acceleration of the reverse flow. The rubber is preferably silicone and a 20%

IMPROVED JET INJECTOR

addition of silicone oil prior to cure to ensure that the valve does not re-seal during storage. The non-return valve may be opened by the syringe piston pressure to deliver the main dose in the normal fashion.

The outer surface of the nozzle may induce a saddle shape in the skin under pressure. Skin is remarkably resistant to biaxial stretching so to ensure that the slit like orifice to the track through the skin is held open, the stress must be anisotropic. Figure 3 shows a nozzle surface, 30, that is essentially conical, 31, with a cylindrical relief, 32, perpendicular to the injector axis. The skin, 33, is extended under pressure by forming around the cylindrical surface. This tension keeps the track entrance, 34, open.

IMPROVED JET INJECTOR

Abstract

PCT / GB 02 / 02633 describes a low cost jet injector. The present specification describes a number of improvements in the device. The spring may be manually cocked and pressure on the skin of the patient may trigger the energy release. The spring may be in the form of one or more C springs deforming by bending solely in the plane of the injector axis. The end thrust beams may comprise a discrete piston that engages with a small cross section cylinder. A small channel provides a simple detent mechanism to retain the spring. The flexible portion of the rigid tube may be formed by having an open window in the rigid tube with a cylindrical shell rubber moulding within the tube. This moulding may be free or bonded onto the end of the constriction. The moulding may also incorporate a non return valve that is normally closed or even biassed closed in the quiescent state. The outer surface of the nozzle may be saddle shaped to keep the track entry open.

IMPROVED JET INJECTOR

Figure 1

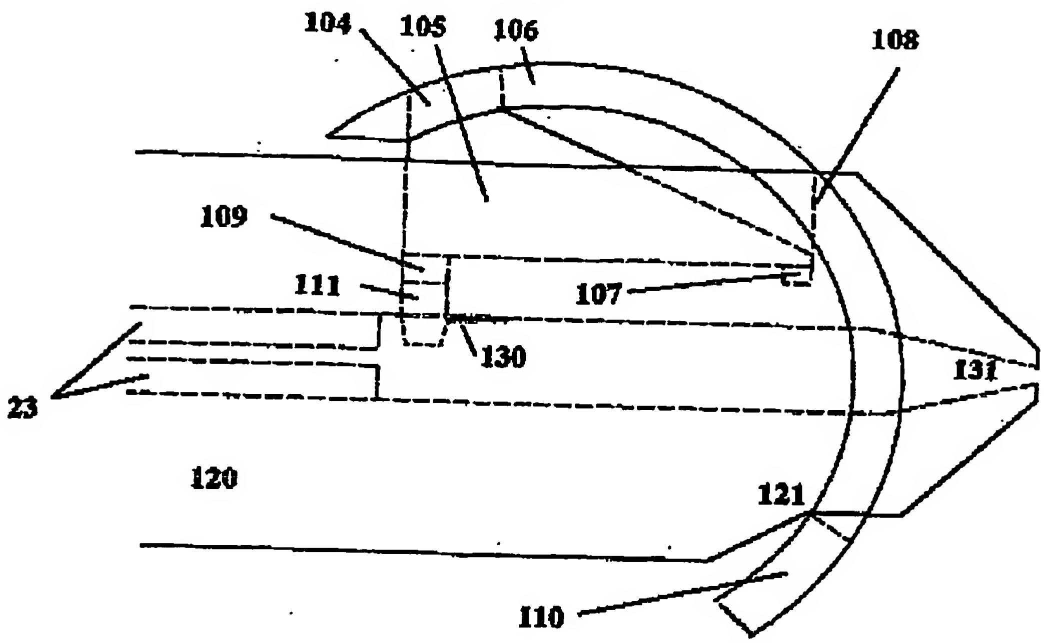
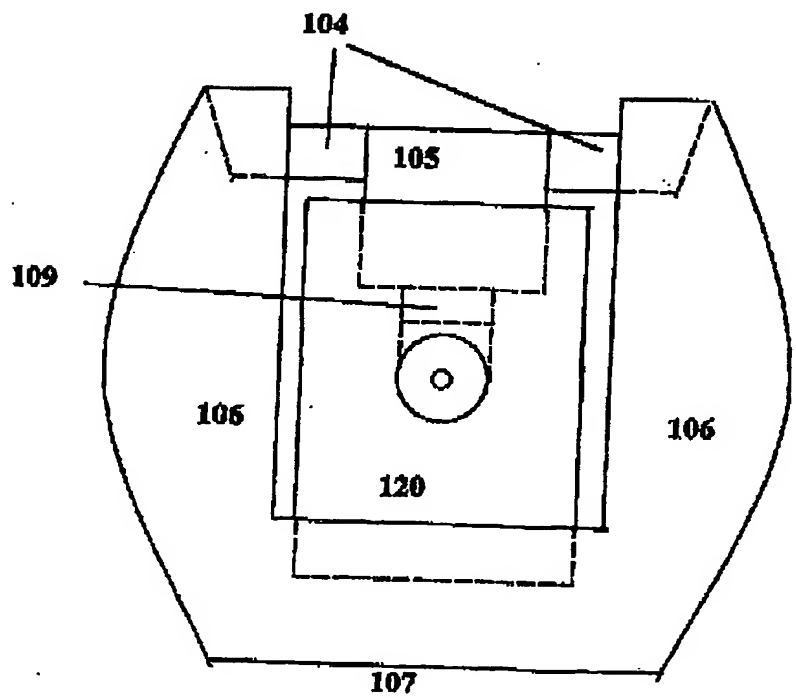


Figure 1a



IMPROVED JET INJECTOR

Figure 1b

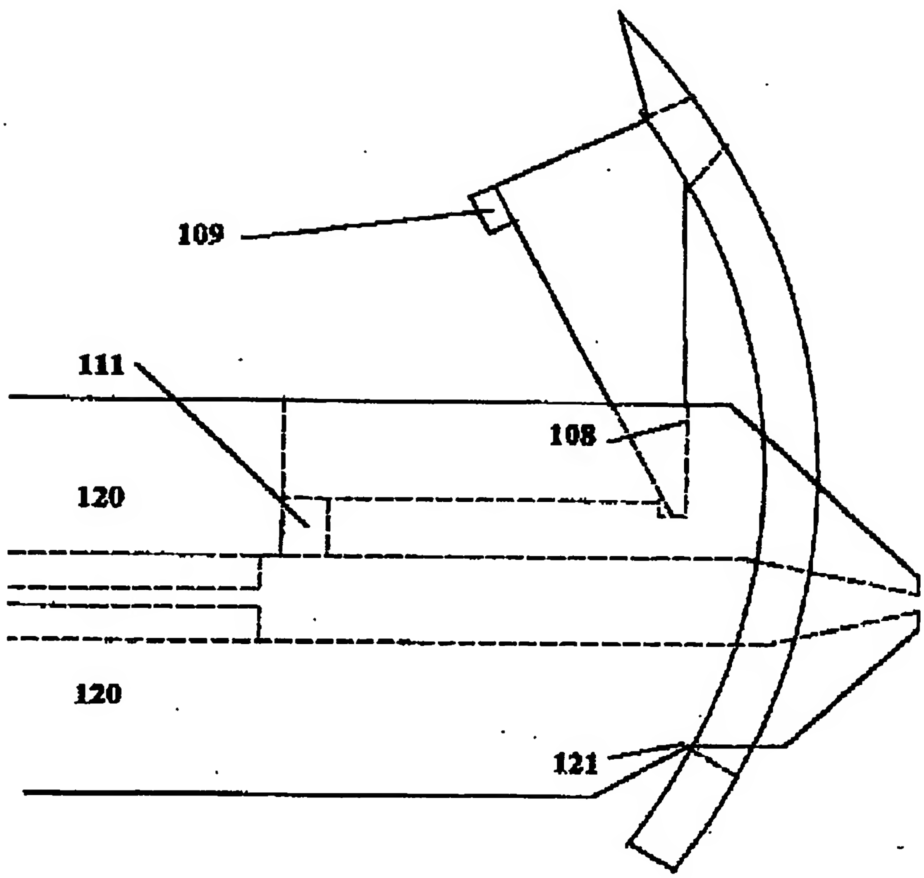


Figure 1c

IMPROVED JET INJECTOR

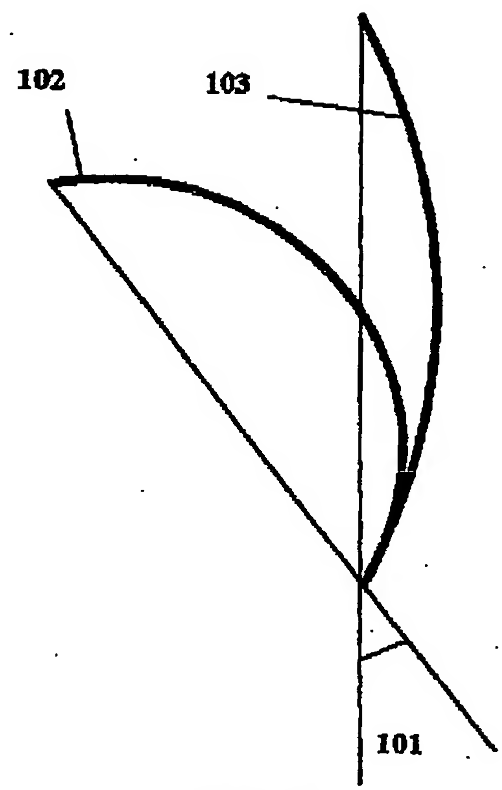


Figure 1d

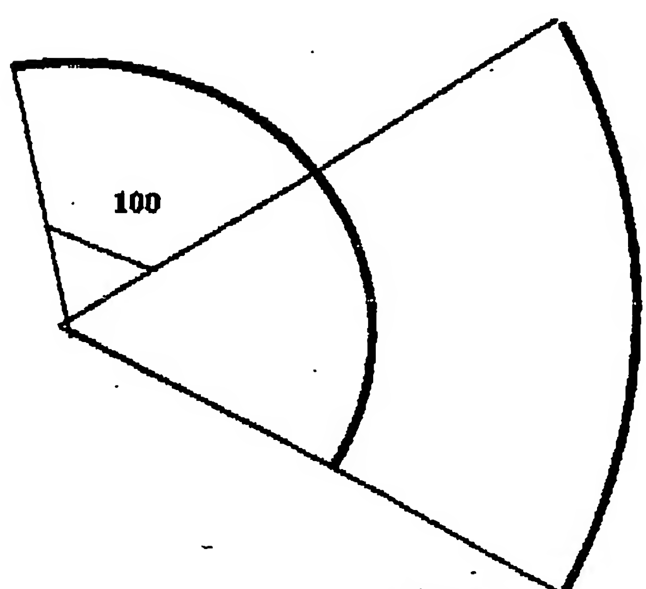


Figure 1e

IMPROVED J[illegible] INJECTOR

Figure 2

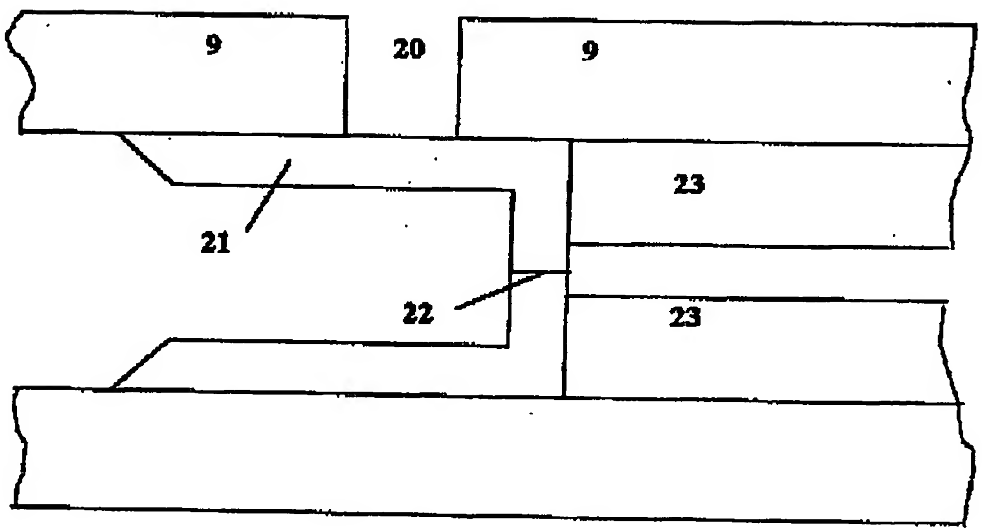
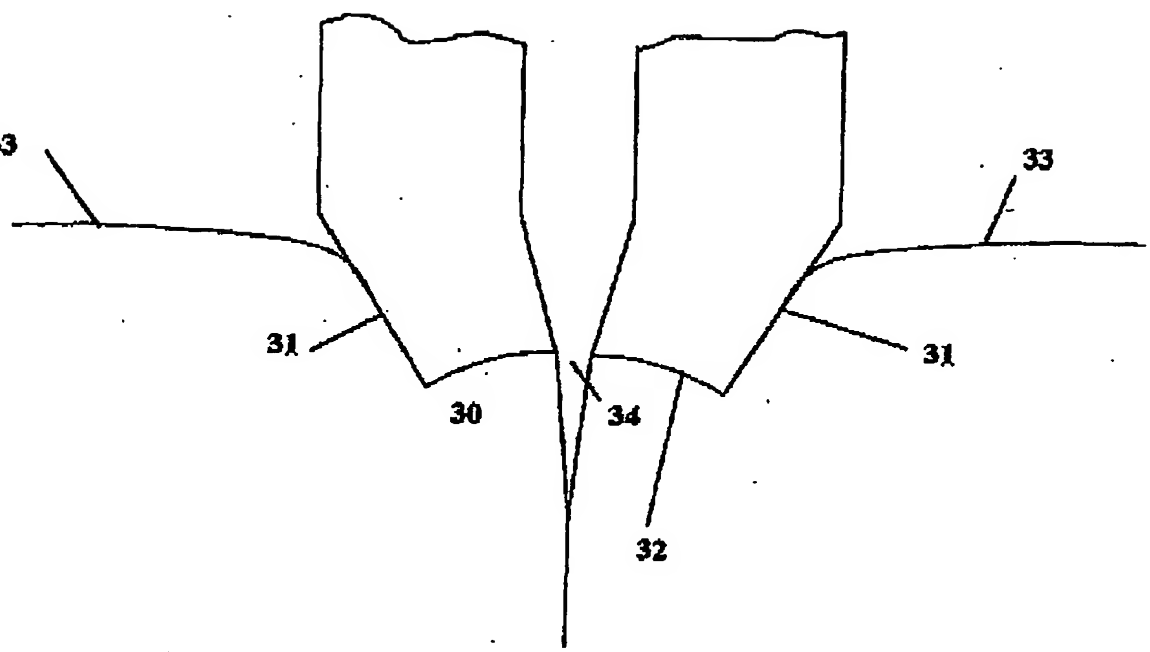


Figure 3



PCT Application
GB0304706